

### **Remarks**

Claims 1-4, 7-14, and 17-19 have been canceled without prejudice to the filing of continuing applications. The abstract of the disclosure has been amended to more accurately reflect the claimed subject matter. Also, claims 20-21 have been amended to correct a typographical error. Objection of claims 20-21 is therefore respectfully requested.

The claims stand rejected under U.S.C. § 112, first paragraph, as not providing enablement for any compound of the claimed structure comprising any biological active molecule. The claims have been amended to reflect only siRNA molecules. Withdrawal of the lack of enablement rejection is therefore respectfully solicited.

Finally, claim 1-4 and 12-14 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 90/12096 (the '096 application) in view of Connolly. Specifically, the '096 application teaches exogenous molecules conjugated to a biotin or folate moiety of the complex. Connolly discloses that synthetic cluster glycosides containing three N-acetylgalactosamine residues bind to cell surface receptors on rabbit hepatocytes and are taken up into the cells by endocytosis. The Examiner contends that it would have been obvious to one of ordinary skill in the art at the time of the invention to produce a conjugate comprising a biologically active molecule conjugated to a cluster of three N-acetylgalactosamine residues by the trivalent linkers of Formulas 119 and 121, attached with the linkers of instant claims 15 and 16. Applicants respectfully disagree.

At the outset it is noted that before a reference can constitute legally cognizable prior art, it must enable what it discloses. Neither the '096 application nor Connolly enables biological molecule conjugates *containing an siRNA*, as is required by the

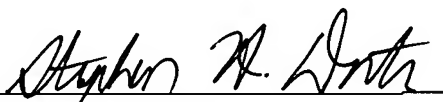
amended claims. At the priority date of the present application, those of ordinary skill in the art understood that there were different structural features of nucleic acids required for activity in each of, for example, antisense, ribozyme, and siRNA technologies because the mechanism of action of these nucleic acids differed in each. Significantly, the mechanism of siRNA had not yet been explored to the extent that one of ordinary skill in the art understood or could predict the effect of a siRNA conjugate of the instant claims. Thus, it would not have been obvious to one skilled in the art at the priority date of the instant invention to combine the '096 application and Connolly to arrive at the present invention. For this reason, withdrawal of the obviousness rejection is respectfully requested.

Claims 10-11 and 20-21 also stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the '096 reference in view of Connolly and further in view of Li. In light of the amendments to the claims and arguments presented above, Applicants respectfully solicit withdrawal of the obviousness rejection.

Allowance of the claims and passage of the case to issue is respectfully solicited. Should the Examiner believe a discussion of this matter would be helpful, he is invited to telephone the undersigned at (312) 913-0001.

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